



**Karolinska
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Institutionen för odontologi

Oral Mucositis and Periodontal Disease in Patients with Primary or Acquired Immunodeficiencies

AKADEMISK AVHANDLING

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av

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ABSTRACT

The infection and inflammation in the oral cavity are commonly related to the skewed interaction between host immunity and inhabiting microorganisms. Both primary and acquired immunodeficiency conditions are frequently associated with oral symptoms. In this thesis two oral manifestations, chronic periodontitis and oral mucositis, were investigated in patients with severe congenital neutropenia and in patients with malignant diseases respectively.

In Paper I, a genotype-phenotype correlation between *ELANE* mutations and chronic periodontal disease was described in a group of patients with severe congenital neutropenia. Patients that harbor mutations in the gene *ELANE*, encoding neutrophil elastase, presented with poorer periodontal health as compared to those with *HAX1* mutations or unknown mutations. The periodontal pockets of the patients with *ELANE* mutations displayed a skewed microflora and elevated levels of proinflammatory cytokine IL-1 β .

In Paper II and III we studied the oral mucositis, an acute side effect frequently encountered during cytostatic chemotherapy, in a group of pediatric patients diagnosed with various types of malignancies. In Paper II, we showed that at the time of malignancy diagnosis, patients with acute leukemia had highest risk of oral mucositis, presenting with high concentrations of inflammatory cytokines IL-6, IL-8, IL-10, and TNF- α and low levels of pro-LL-37 (hCAP-18) in the blood plasma. In Paper III we conducted high-throughput sequencing of the oral mucosal bacterial community in an attempt to investigate the role of bacteria in the pathogenesis of oral mucositis development. At the time of malignancy diagnosis, patients who later developed oral mucositis were found to have higher oral mucosal microbial diversity and were more heterogeneous among one another compared to those that did not develop mucositis. A more pronounced modification of the bacterial community by chemotherapy was detected in patients that later developed oral mucositis, indicating a beneficial role of stable oral microbiota.

In the last paper of this thesis, we investigated the variation of blood pro-LL-37 levels in a cohort of patients presenting with chronic neutropenia. The lower values of pro-LL-37 were found in cases with severe congenital neutropenia, as compared to autoimmune, idiopathic, and ethnic neutropenia. The findings support the view that benign forms of neutropenia could be distinguished from the severe forms at an early stage. Plasma pro-LL-37 levels may potentially work as a diagnostic parameter and this analysis could be developed for clinical use.

Providing adequate and personalized oral care to the patients with immunodeficiencies has necessitated more knowledge regarding the predisposition and pathobiology of their oral manifestations. The findings in this thesis may benefit the clinical management and subsequently improves the patient's quality of life.